

REMARKS

Claims 38, 39, and 41-61 are currently pending in this application.

No claim amendments are made with this paper, and no new matter has been introduced.

Applicants expressly reserve the right to pursue any non-elected, canceled or otherwise unclaimed subject matter in one or more continuation, continuation-in-part, or divisional applications.

Reconsideration and withdrawal of the objections and the rejections of the present application in view of the remarks herein, is respectfully requested, as the application is in condition for allowance.

Priority

Applicants note with appreciation that the Office acknowledges Applicants' claim for foreign priority under 35 U.S.C. § 119(a)-(d). The *Action* also indicates the receipt of the certified copies of the priority documents from the International Bureau. As such, Applicants thank the Examiner.

Rejections under 35 U.S.C. §103(a)

Claims 38, 39, 41-45, 47-49, and 52-61 have been rejected under 35 U.S.C. §103(a) as allegedly rendered obvious over WO 96/03768 to Vestal *et al.* (hereinafter "Vestal") in view of U.S. Patent Publication No. 2004/0119010 to Perryman *et al.* (hereinafter "Perryman"). In particular, the Examiner alleges that it is obvious to one skilled in the art to arrive at the claimed subject matter of this application by combining the analysis method of Vestal with appropriate matrix materials disclosed in Perryman (*see* page 4 of the *Action*). Applicants respectfully traverse.

The instant claims are directed to methods of quantifying simultaneously a plurality of elements in a fluid sample adsorbed/absorbed onto or into a solid inert collection matrix (as recited in claims 38 and 39, and claims dependent therefrom). It is submitted that, according to the methods as presently claimed, a sample is prepared by adsorbing/absorbing the sample onto or into the inert collection matrix that is in a pre-

prepared solid form. As such, there is no additional treatment (such as drying) needed in the sample preparation.

In contrast, Vestal discloses a sample preparation method that differs significantly from the methods of pending claims. Vestal discusses sample preparation by loading the sample into a liquid solution and then allowing the resulting mixture to dry (*see*, e.g., lines 4-6 at page 6 of Vestal). Vestal does not require the sample be mixed with a matrix, and does not teach or suggest adsorbing and/or absorbing the sample onto or into a solid inert collection matrix as required in the presently-claimed methods. Furthermore, Vestal requires a step of drying in its sample preparation.

Applicants note that Vestal may have mentioned sample preparation wherein a matrix is used. However, Vestal requires that the matrix used in the preparation is in a solution when being mixed with the sample solution (*see*, e.g., lines 20-23 at page 1, and lines 5-10 at page 10 of Vestal). As such, Applicants submit that Vestal fails to teach or suggest each and every element of the claimed subject matter of this application, such as, a step of adsorbing/absorbing a sample onto or into an inert collection matrix that is solid. Accordingly, one skilled in the art would appreciate the methods disclosed in Vestal and in this application are patentably distinct from each other, partially due to the significant differences in the sample preparation procedures.

Applicants further submit that Vestal fails to provide any motivation or suggestion to a skilled artisan to modify the methods therein to reach the presently-claimed subject matter. As above discussed, Vestal only teaches sample preparation through loading the samples into a liquid solution and then allowing the resulting mixture to dry. Vestal does not mention at all any pre-prepared solid matrix that is used to adsorb/absorb the sample (as recited in the instant claims). Further, Vestal clearly favors in obtaining a sample/matrix solution by highly preferring a computer-controlled system wherein the resulting sample/matrix solution is dried “in an environment in which the pressure, temperature, and composition of the surrounding atmosphere is controlled” (*see* lines 9-12 on page 11 of Vestal). Indeed, one skilled in the art would not be motivated to come up with the claimed methods of this application based on Vestal’s disclosure.

At least for the reasons stated above, Applicants submit that the claimed subject matter of this application is patentable over Vestal.

Applicants further submit that the addition of Perryman does not and cannot remedy the deficiencies of Vestal. While the *Action* at page 4 points Paragraphs 57 and 123-126 of Perryman (discussing using solid organic acids as matrix materials and also using a crystallization method in sample preparation), Perryman does not teach or suggest an analysis method which requires adsorbing/absorbing a sample onto or into a solid inert collection matrix that is pre-prepared. Instead, Perryman only teaches sample preparation methods that require using a solution of matrix. For example, the “E. crystallization methods” or “the dried droplet method” taught in Perryman require that the matrix material is prepared in a “fresh saturated solution” before being mixed with a sample solution to form a mixture droplet, and that the droplet is then dried (see Paragraphs 122 through 134 of Perryman). Further, the “fast evaporation method” disclosed in Perryman requires a preparation of a “matrix-only solution,” in which the matrix material is dissolved in acetone containing water or TFA, and that the matrix solution is then added to a sample stage, resulting in a matrix surface for sample addition (see Paragraphs 169 through 176 of Perryman).

Additionally, Applicants note that other preparation methods disclosed in Perryman are developed based on either “the dried droplet method” or “the fast evaporation method” or both (see, e.g., Paragraphs 166, 183, and 193 of Perryman). Perryman simply does not teach or suggest a sample preparation method in which the sample is adsorbed/absorbed onto or into a solid matrix which is pre-prepared, let alone teaching a solid inert collection matrix as recited in the instant claims.

Applicants further submit that Perryman also fails to provide any motivation or suggestion to a skilled artisan in modifying its methods to arrive at the claimed methods of this application. As such, Perryman does not teach or suggest using a solid pre-prepared matrix for sample preparations. Instead, a skilled artisan would favor using a matrix solution for a sample preparation based on Perryman’s teaching.

Additionally, Applicants note that the fast evaporation method disclosed in Perryman is not suitable for analysis of mixtures or biological fluids (in contrast to the presently-claimed methods; see, e.g., claims 52 and 53). In particular, Perryman states that the fast evaporation method is unable to provide reproducible sample-to-sample data for peptides and protein mixtures or a bodily fluid (see, e.g., paragraph 181 of

Perryman). In contrast, the methods disclosed in the present application can be used for analysis of a wide variety of fluid samples (*see, e.g.*, lines 6-10 at page 5, Experiments 5, 13, and 18, of this application).

Thus, Applicants submit that Vestal, whether considered alone or in combination with Perryman, does not teach or suggest each and every element of the presently-claimed subject matter. There is no suggestion or motivation either in Vestal or Perryman to modify the methods therein to arrive at the claimed methods, nor is there a reasonable expectation of success in the art to achieve desirable technical results of the claimed methods. Therefore, Applicants respectfully contend that the presently claimed subject matter is patentable over Vestal in view of Perryman.

At least for the foregoing reasons, Applicants respectfully request that the rejections under 35 U.S.C. § 103(a) of claims 38, 39, 41-45, 47-49, and 52-61 be withdrawn.

Claim 46 has been rejected under 35 U.S.C. §103(a) as allegedly rendered obvious over Vestal in view of "Structure of a Matrix Based on Polysaccharide Derivatives for the Immobilization of Biologically Active Substances" to Burkhanova *et al.* (hereinafter "Burkhanova"). In particular, the Examiner alleges that it is obvious to one skilled in the art to reach the presently-claimed subject matter by using the matrix modification disclosed in Burkhanova to modify the Vestal matrix (*see* page 7 of the *Action*). Applicants respectfully traverse.

Pending claim 46 further recites that the fibrous cellulose used as a collection matrix in the presently-claimed methods is modified by oxidation and/or acid hydrolysis. For reasons including those delineated above, Applicants submit that Vestal does not teach or suggest each and every element of the claimed subject matter of this application (*e.g.*, a step for adsorbing/absorbing a sample onto or into a solid inert collection matrix), and that Vestal does not provide any suggestion or motivation to a skilled artisan to modify the method disclosed therein in order to arrive at the claimed methods. Accordingly, Vestal does not render obvious Applicants' claimed subject matter.

Moreover, Applicants submit that the combination of Burkhanova fails to cure the deficiencies of Vestal, as Burkhanova does not teach or suggest elements of Applicants' claimed subject matter that Vestal fails to teach (e.g., a step for adsorbing/absorbing a sample onto or into a solid inert collection matrix). It is also submitted that Burkhanova does not provide any suggestion or motivation to a skilled artisan in order to reach the presently-claimed subject matter.

Accordingly, Applicants submit that Vestal, either alone or in combination with Burkhanova, does not establish a *prima facie* case of obviousness of Applicants' presently-claimed subject matter. As such, Applicants respectfully request that the rejection of claim 46 be withdrawn.

Claims 50-51 have been rejected under 35 U.S.C. §103(a) as allegedly rendered obvious over Vestal in view of U.S. Patent No. 5,777,324 to Hillenkamp *et al.* (hereinafter "Hillenkamp"). More specifically, the Examiner alleges that it is obvious to a skilled artisan to reach the claimed subject matter by combining a porous or fibrous matrix cover disclosed in Hillenkamp with the method disclosed in Vestal (*see* page 8 of the *Action*). Applicants respectfully traverse.

The instant claims further recite that: the claimed methods of the application use a sample collection device that further comprises an integral or separate matrix cover sheath (claim 50); and the sample collection device used has multi-layers where the collection matrix layer is sandwiched between two supporting layers with one having an opening exposing the collection matrix (claim 51).

For reasons including those delineated above, Applicants submit that Vestal does not teach or suggest each and every element of Applicants' claimed subject matter (e.g., a step for adsorbing/absorbing a sample onto or into a solid inert collection matrix), and that Vestal does not provide any suggestion or motivation to a skilled artisan to modify the method therein to arrive at the presently-claimed methods. Accordingly, Applicants submit that Vestal does not render obvious the presently-claimed subject matter.

Moreover, Applicants submit that Hillenkamp fails to cure the deficiencies of Vestal, as Hillenkamp also fails in teaching or suggesting the elements of Applicants'

claimed subject matter that Vestal fails to teach (e.g., a step for adsorbing/absorbing a sample onto or into a solid inert collection matrix). Additionally, Hillenkamp also fails in providing any suggestion or motivation to a skilled artisan to modify the methods therein to arrive at the presently-claimed methods.

Accordingly, Applicants submit that Vestal, either considered alone or in combination with Hillenkamp, does not establish a *prima facie* case of obviousness of the presently-claimed subject matter. Therefore, Applicants respectfully contend that the rejection under 35 U.S.C. § 103(a) of claims 50-51 is improper and should be withdrawn.

CONCLUSIONS

For at least the foregoing reasons, the present application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are respectfully requested.

Applicants request any extension of time necessary for consideration of this response. Please charge any required fee or credit any overpayment to Deposit Account No. 04-1105, under Order No. 62302(70403).

If the Examiner believes that a telephone conversation with Applicants' attorney/agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney.

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Respectfully submitted,

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